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Review Article

Chondrosarcoma of thalamus: report of a pediatric case with review of literature

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Abstract: This study aimed to report unusual location and imaging findings of an intracranial chondrosarcoma in a 7-year-old child. Chondrosarcoma is a malignant tumor arising from the chondrocytes that remain at the synchondroses of basilar skull bones. It is difficult to differentiate chondrosarcoma from chordoma because they are similar in appearance. The prognosis and survival rate of patients depend on the pathological type and degree of resection of tumors. In this study, the patient was in a comatose state on admission. The computed tomography and magnetic resonance imaging of the head revealed a mass lesion extending from the left thalamus to the left cerebellar peduncle, and the imaging findings looked like a granulomatous sphere from fungal infection. The mass lesion was completely resected, and chondrosarcoma was diagnosed after pathological examinations. This tumor was present in an unusual location, compared with most chondrosarcoma cases, with atypical imaging findings, hindering the diagnosis of this intracranial chondrosarcoma case on admission. Also, this study reviewed the incidence of intracranial chondrosarcoma in children since 1963 and analyzed the treatment modalities related to the prognosis. The study showed that the prognosis and survival rate of patients with chondrosarcoma depended on the pathological type and treatment modalities.

Keywords: Chondrosarcoma, thalamus tumor, pediatric

Introduction

Chondrosarcoma is a malignant tumor comprising cartilage-producing cells. It represents 0.15% of all intracranial tumors and 6% of all skull base tumors; 75% of intracranial chondrosarcomas are located at the skull base [1, 2]. Chondrosarcomas originating from the skull base occur mainly in the area where the chondrocranium is formed, such as petrous apex, posteromedial temporal bone, and between the internal acoustic meatus and the jugular foramen [3-7]. Normally, the tumor is located in the skull base area. In such cases, patients usually present with headaches, cranial nerve palsies, hearing deficits, and gait disturbances [8]. The differential diagnosis of this tumor is mainly chordoma because of the similarities in location, symptoms, and imaging appearances [6, 9]. Chondrosarcoma is difficult to differentiate from meningioma in unusual locations such as falcine or parasagittal area [3, 10]. This tumor may also be found in patients with Ollier's disease, Maffucci syndrome, Paget's disease, and osteochondrosarcoma. However, in most cases, this tumor arises *de novo* [11].

Surgery remains the first treatment choice for intracranial chondrosarcoma. Postoperative adjuvant radiotherapy and stereotactic radiotherapy may be effective. However, the efficacy of this treatment in reducing tumor residue and tumor recurrence is still widely debated [12]. The prognosis of a patient is related to the pathological subtype, degree of tumor resection, and adjuvant postoperative radiation therapy [1]. This study presented a case of chondrosarcoma in the pediatric population. The tumor, in this case, had an unusual presentation of location and radiological findings, compared with most cases reported in the previous literature. Chondrosarcoma was not confirmed in a primary diagnosis until the histological examination result was obtained.

Case presentation

Initial presentation and management

This study was approved ethically by the Beijing Tiantan Hospital Affiliated to the Capital Medical University. The patient and his next-of-kin provided informed written consent for the publication of this case report.

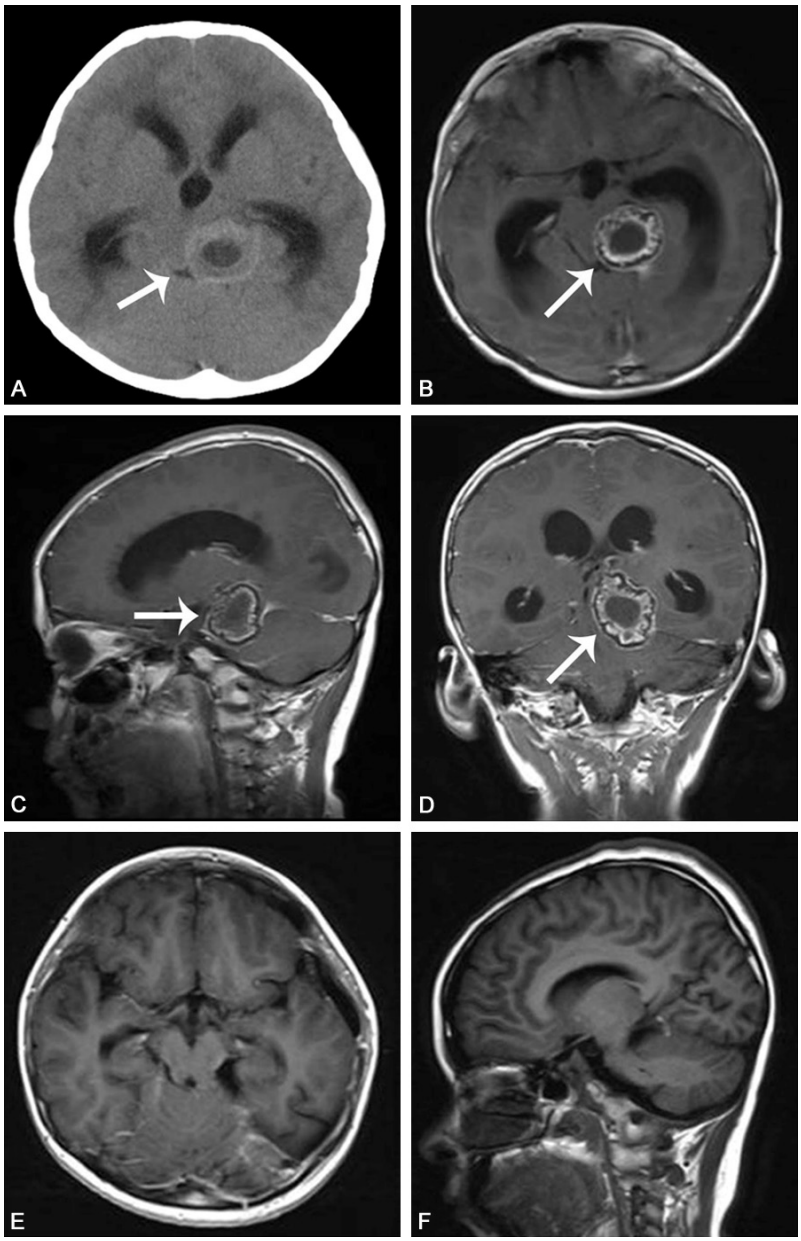

Figure 1. Radiographic features of chondrosarcoma on CT and MRI scan. The patient presented with a 30 × 27 × 38 mm^3 lesion extending from the thalamus to the brain stem. A. Noncontrast axial CT scan of the lesion showing central hypodensity, most likely representing areas of necrosis. B-D. Gadolinium contrast enhancement showing unusual imaging appearances of chondrosarcoma; a cystic cavity at the center of the mass lesion and hyperintensity at the peripheral mass lesion were observed; the mass lesion appeared to be a granulomatous disease accompanied by fungal infection. E, F. Postoperative MRI scans showing the total removal of mass lesion.

A 7-year-old male patient presented with a history of persistent headache and numbness on right extremities for about 1 month. The headache was described as persistent distending pain, without vomiting, nausea, or fever at the onset of symptoms. Physical and neurological examinations were unremarkable. At first, the patient was diagnosed with encephalitis at a local hospital. Antibiotic and fluid infusions did not alleviate the symptoms. The consciousness of the patient dramatically worsened 15 days after the prescription of medicines. Magnetic resonance imaging (MRI) of the head was performed, which showed an occupied mass lesion accompanied by obstructing hydrocephalus. Mannitol and fluid infusions were given. Doctor from the local hospital suggested surgical treatment, and the patient was brought to the Beijing Tiantan Hospital for further treatment.

The patient was in a comatose state on admission, with the body temperature of 36.7°C and the blood pressure of 129/84 mmHg. He did have normal respiration and heart rates. Blood serum and cerebrospinal fluid (CSF) tests showed no abnormal findings. MRI and computed tomography (CT) of the head showed hydrocephalus, and a mass lesion of 30 × 27 × 38 mm^3 extending from the left thalamus to the left cerebellar peduncle. The gadolinium contrast enhancement showed unusual imaging appearances of chondrosarcoma. A cystic cavity at the center of the mass lesion and hyperintensity at the peripheral mass lesion were observed (**Figure 1A-D**). An extraventricular drain was urgently placed to relieve the high intracranial pressure. After the procedure, the patient gradually regained his consciousness.

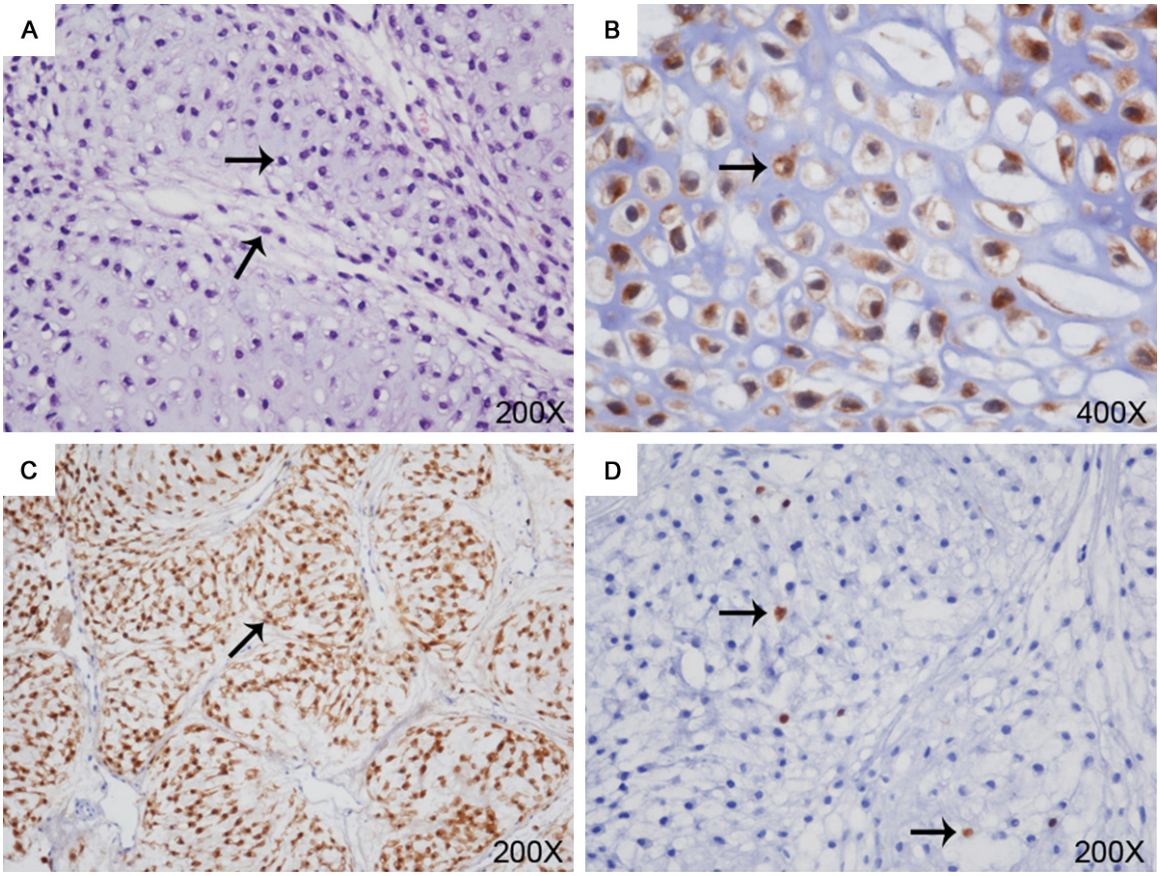

Figure 2. A. A hyaline tumor of low-to-moderate cellularity with mild variation in size and shape of the tumor cells, showing mild nuclear pleomorphism (pointed by arrow) (hematoxylin and eosin staining, 200 ×, pointed by arrow). Immunohistochemical staining showed that the cells of the chondrosarcoma were: B. Negative cell nucleus reactivity for Brachyury but positive staining for cytoplasm (pointed by arrow) (400 ×); C. Strong nuclear reactivity for S-100 protein (pointed by arrow) (200 ×); D. Some Ki67 positivity (pointed by arrow) (200 ×).

Two days later, a temporoparietal craniotomy was performed, and the mass lesion was reached through the median fossa approach. The cerebellar tentorium was exposed after gentle retraction of the temporal lobe. The tumor appeared to bulge to the cerebellar tentorium. It was a gray-white solid mass, which was slightly rigid and tenacious. A cystic change inside the mass was observed, with the cystic cavity filled with a yellowish fluid. The lesion had a clear border with the surrounding tissue and a moderate blood supply. The tumor was resected piece by piece until the whole tumor was completely removed (**Figure 1E** and **1F**). The trochlear and oculomotor nerves were preserved well during the removal of the tumor.

The patient gradually recovered and was eventually discharged from the hospital after 3 weeks, and no adjuvant therapy was given. The patient was followed up by 6 months (**Figure 3A-C**) and 1 year (**Figure 3D** and **3F**) after the surgery. The MRI scan showed no tumor recurrence. The patient had a good recovery without any neurological deficit.

Histopathology findings

The histological analysis showed a hyaline tumor of low-to-moderate cellularity, with mild variation in size and shape of the tumor cells, showing mild nuclear pleomorphism. Immunostaining revealed a strong nuclear reactivity for S-100 protein indicative of a cartilaginous tumor. Some Ki67 positivity and negative cell nucleus reactivity for Brachyury confirmed the diagnosis of chondrosarcoma (**Figure 2**).

Discussion

Intracranial chondrosarcomas represent about 0.15% of all intracranial tumors [5, 38, 39]. The

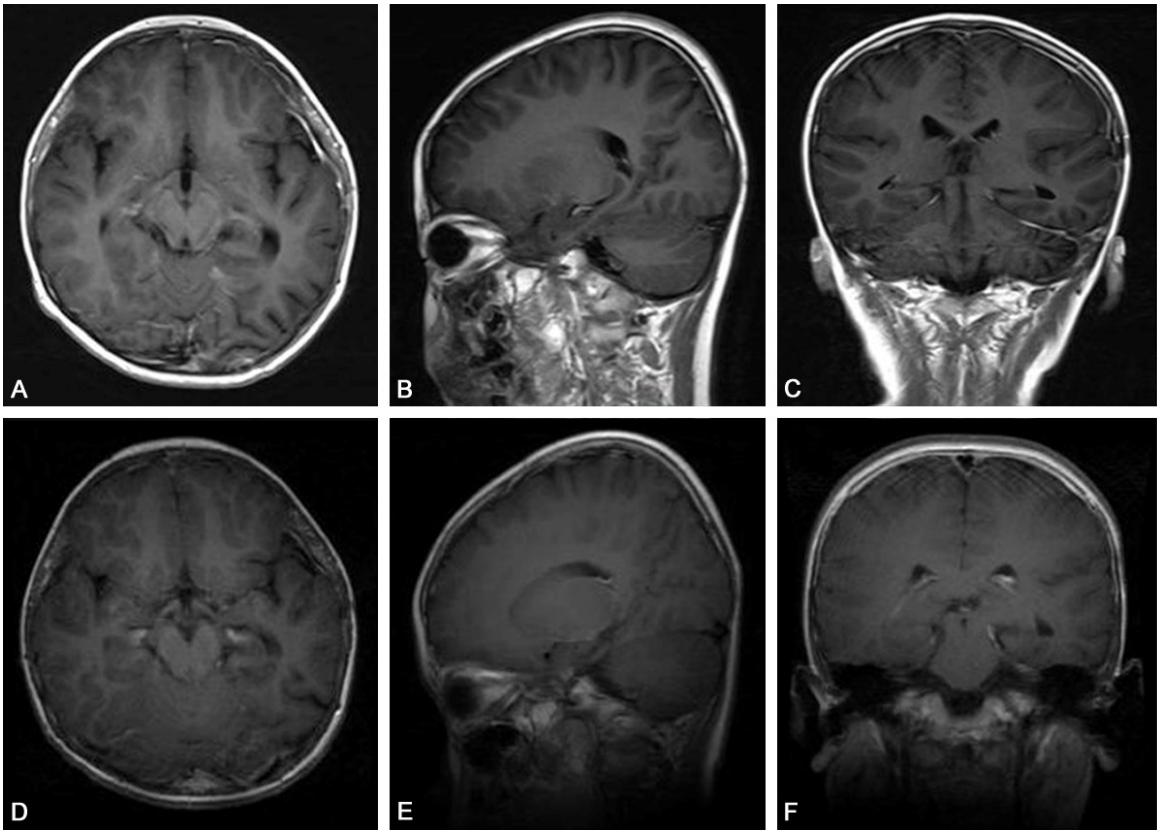

Figure 3. MRI scans showed no tumor recurrence at 6 months (A-C) and 1 year (D-F) after the surgery.

majority of these lesions arise from chondrocytes that remain at the synchondroses of basilar skull bones [4]. Chondrosarcoma is extremely challenging to differentiate from chordoma. Despite similarities in the appearance of chondrosarcoma and chordoma, studies showed that 5- and 10-year survival rates after diagnosing chondrosarcoma were considerably higher than those after chordoma [8, 40]. Chondrosarcoma occasionally arises in the extraosseous region and may be misdiagnosed as meningioma [41, 42]. Hyperostosis caused by the erosion of the bone because of the tumor in some cases and the rare presence of the dural tail in chondrosarcoma may be the interference factors misleading the cause in diagnosis [3, 10].

Granulomatous disease accompanied by fungal infection was presumed rather than meningioma in the primary diagnosis based on CT and MRI examinations, although the evidence was not supportive enough for both. In the present case, meningioma was not considered in the primary diagnosis because of the absence of a dural tail sign on gadolinium contrast enhancement. The CT finding of chondrosarcoma is usually isoattenuated to hyperattenuated, with variable degrees of heterogenous enhancement and calcification often present in most cases. MRI findings showed that this tumor was frequently hypointense on T1-weighted imaging (T1WI) and hyperintense on T2WI, and contrast enhancement might be mild or moderate and described as a “honeycomb” pattern [2, 3, 6, 27, 43, 44]. CT scans revealed that the lesion appeared as ischemic areas or focal infarctions, as seen in some cerebral fungal infections [45]. In rare cases, the MRI examination might indicate a cerebral abscess. The patient developed fever, and the CSF showed nervous system infection. This evidence implied that granulomatous disease accompanied by fungal infection had a higher probability compared with the intracranial tumor. The other reason was that the tumor was located at the cerebellar tentorium. This is unusual for chondrosarcoma; most chondrosarcomas are located at the petroclival junction, as reported by previous studies [1]. However, the cystic cavity

Table 1. Retrospective study of 32 patients with pediatric chondrosarcoma

No	Author	Year	Age/ Sex	Location	Pathology	Treatment	Follow up (months)	Outcome
1	Flyger et al [13]	1963	11/F	Right frontal	Mesenchymal	S	5	Alive
2	Wu et al [14]	1970	18/F	Frontal	Mesenchymal	S	14	Died
3	Lynch et al [15]	1973	13/M	Right frontoparietal	Mesenchymal	S	18	Alive
4	Guccion et al [16]	1973	19/M	Parietal	Mesenchymal	S, RT	12	Alive
5	Zucker et al [17]	1978	19/M	Occipital	Mesenchymal	S	N/A	N/A
6	Scheithauer et al [18]	1978	7/M	Right temporal	Mesenchymal	S	84	Alive
7	Rollo et al [19]	1979	11/M	Left parietooccipital	Mesenchymal	S	96	Alive
8	Kobayashi et al [20]	1980	11/F	Parietal	Mesenchymal	S	216	Died
9	Smith et al [21]	1981	12/M	Posterior cranial fossa	Mixoid	S	13	N/A
10	Hoshino et al [22]	1981	14/F	Parietal	Mesenchymal	S, RT	N/A	N/A
11	Kubota T et al [23]	1982	19/M	Parietal	Mesenchymal	S, RT	12	Alive
12	Schut L et al [24]	1983	11/M	Right frontal	Mesenchymal	S, RT	N/A	Died
		1983	12/F	Prefrontal	Mesenchymal	S, RT, C	N/A	Died
13	Parker et al [25]	1989	6/F	Thalamus	Mesenchymal	None	96	Died
14	Chhem RK et al [26]	1992	11/F	Left parietal	Mesenchymal	S, RT	18	Alive
15	Cho et al [27]	1993	13/F	Left frontoparietal	Mesenchymal	S	36	Alive
16	Rushing et al [28]	1996	5/M	Frontal	Mesenchymal	S, RT	14	Alive
			7/F	Sphenoid ridge	Mesenchymal	S	60	Died
			11/F	Frontal	Mesenchymal	S, RT	20	Died
			13/F	Sphenoid ridge	Mesenchymal	S	15	Alive
			15/M	Parasagittal	Mesenchymal	S, RT	72	Died
			17/F	Anterior skul base	Mesenchymal	S, RT	84	Died
17	Malik et al [29]	1996	8/M	Cerebellar parenchyma	Mesenchymal	S, RT, C	18	Alive
18	Nozaki et al [30]	1999	15/M	Jugular foramen	Mesenchymal	S, RT	35	Alive
19	Crosswell et al [31]	2000	0.5/M	Right frontoparietal	Mesenchymal	S, C	2	Died
20	Marshman et al [32]	2001	17/F	Right parietal	Mesenchymal	S, RT	4	Died
21	Gonzales et al [33]	2002	17/F	Right frontoparietal	Mixoid	S	35	N/A
22	La Spina et al [34]	2003	14/F	Parietal	Mesenchymal	S	24	Alive
23	Chen et al [35]	2004	13/F	Frontal	Mesenchymal	S	N/A	N/A
24	De Cecio R et al [36]	2008	0.16/M	Parietal	Mesenchymal	S	Few weeks	Died
25	Sardi et al [37]	2010	16	Frontal	Mesenchymal	S, RT, C	55	Alive
			9	Infratentorial	Mesenchymal	S, RT, C	33	Alive
26	Present case	2016	7/M	Cerebellar tentorial	Dedifferentiated	S	12	Alive

Abbreviations: C, Chemotherapy; N/A, not available; RT, radiotherapy; S, surgery.

was found to be filled with a yellowish fluid during the surgery. At that time, the lesion was presumed to be an intracranial tumor with hemorrhage, a rare case of chondrosarcoma presenting with hemorrhage, as reported by previous studies [46, 47]. The presence of the yellow fluid could possibly be the hemosiderin deposition due to intratumoral hemorrhage. It is difficult to differentiate chondrosarcoma from chordoma or meningioma or granulomatous disease accompanied by fungal infection unless the histological result is obtained. A better understanding of the imaging study and a complete examination during admission and hospitalization should be integrated and considered for further diagnosis.

Chondrosarcoma and chondroma are difficult to differentiate because of many similarities in their pathological examination. However, recent studies suggest that Brachyury-negative staining is a marker of chondrosarcoma rather than of chondroma [48-50]. The combination of specific microscopic findings, Brachyury-negative nuclear staining, strong positive staining of S-100, and some Ki67-positive staining led to the diagnosis of chondrosarcoma in the present case.

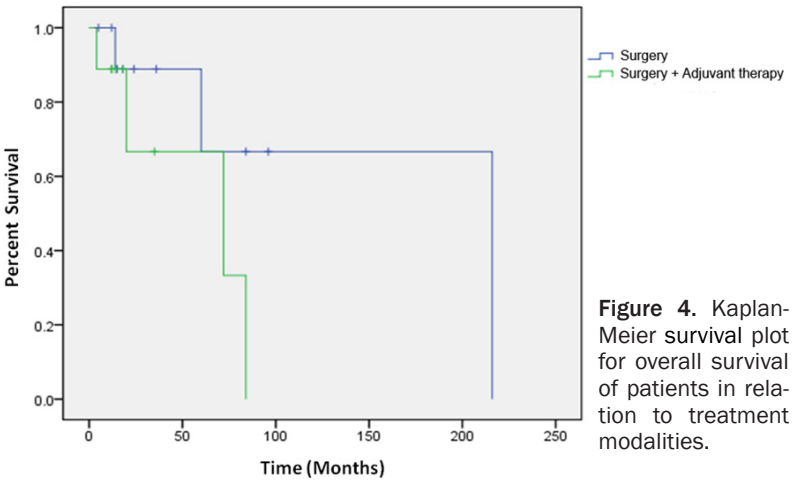

Figure 4. Kaplan-Meier survival plot for overall survival of patients in relation to treatment modalities.

The prognosis and survival rate of this tumor were influenced by several factors, such as pathological characteristic of the tumor, degree of tumor resection, and postoperative radiotherapy. A retrospective study by Bloch et al showed that the conventional type had a higher survival rate compared with the mesenchymal type. The study also showed that surgery combined with radiation therapy could increase the survival rate in patients with chondrosarcoma [1, 51, 52]. Other studies reported the benefit of radiosurgery for controlling local tumor recurrence. The result of the radiation therapy was also found to be dependent on the histological characteristics of the tumor. However, previous studies reported that the higher the grade of the tumor, the less effective the radiation therapy. Another disadvantage of postoperative radiotherapy is that it may increase the morbidity of patients in a higher-grade tumor [42]. In most cases, completely removing the skull base tumor can be challenging due to the connection of the tumor with the important nerves and vascular structure in the skull base area. The role of radiotherapy is considerable in such cases [53]. However, the need for adjuvant radiotherapy in chondrosarcoma is still debatable. Several studies also reported that chondrosarcomas are radioresistant. However, radiation therapy is still recommended as a palliative treatment for inoperable cases [54-56]. Recently, a study by Kim et al concluded that surgical resection is the gold standard treatment for chondrosarcoma, and radiation therapy is recommended for the tumor that cannot be resected completely and leaves a remnant after the surgery. In chondrosarcoma cases that do not respond to radiation therapy, stereotactic radiotherapy with promising results can be considered as a valuable management option. It can prolong the survival rate and control the local recurrence of the tumor [57]. Published papers in PubMed with the key word "intracranial chondrosarcoma" were reviewed, and 32 patients with intracranial chondrosarcoma were found in the pediatric population (age <18 years) (**Table 1**). The Kaplan-Meier survival analysis was used to compare the survival time of different treatments (**Figure 4**). The analysis showed no statistical difference in the survival duration between surgery and surgery combined with radiotherapy (log-rank = 2.266, $P = 0.132$, $P > 0.05$). Therefore, it was concluded that radiotherapy could be used in the case of a tumor residue. However, if a complete resection can be achieved, radiotherapy is not suggested. The patient did not have any radiation therapy after the operation in the present case, and no tumor recurrence was observed at 1-year follow-up after the surgical treatment.

Conclusions

Chondrosarcoma is a malignant intracranial tumor mainly located in the skull base area. Calcification is seen on most chondrosarcomas in imaging studies. The present case had an unusual location of the chondrosarcoma at the cerebellar tentorium, and the unusual findings on imaging study misled the diagnosis of chondrosarcoma during admission. Intratumoral hemorrhage may occur in chondrosarcoma, although the odds of occurrence are small. A complete examination and a good understanding of imaging study are needed. Diagnosis should be supported by pathological examination. Radiotherapy is not suggested if the tumor is completely removed.

Disclosure of conflict of interest

None.

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